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HUMAN UTERUS IN PREGNANCY, AS IT CAN BE MONITORED BY DSC EXAMINATION
A preliminary study

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The myometrium is the main component in enlargement of uterus and plays essential role in labour contraction. Its physiologic and elastic state has a decisive role in the labour process. We have made the first attempt to find correlation between the thermal parameters of uterus and progress of gravidity. Significant differences were observed between cyclic, non-pregnant and postmenopausal state (0.69 and 0.98 J g^{-1} calorimetric enthalpy as well as 60.6 and 63.1°C for T_m), as well as among the different gestational stages and complications. In case of twin pregnancy and dystocia we have found extremities: 0.37 and 1.34 J g^{-1} calorimetric enthalpies, with 62 and 61.6°C melting temperatures. DSC method seems to be promising tool to follow and understand different molecular changes in the myometrium during pregnancy and its complication of human labour.

Keywords: *DSC, human uterus, myometrium, pregnancy*

Introduction

Principal function of myometrium, the muscular wall of the uterus, is to provide protective environment for fetus during the pregnancy and labour. The uterus can achieve 500- to 1000-fold greater capacity during pregnancy, its mass increases from 50–1100 g [1]. The myometrium is the main component in enlargement of uterus and plays essential role in labour contraction. The myometrium is in relative quiescent state during much of pregnancy, then at onset of labour phasic contractions are developed.

To know the exact mechanism and regulation of myometrial function during pregnancy and labour may aid to predict, prevent and treat different pathological functions, such as premature labour, dysfunctional labour or postpartum uterine atony.

According to our present knowledge endocrine, paracrine and mechanical factors are involved in the regulation of myometrial function, neither of them are fully understood [2–6].

The endocrine regulatory function of sexual steroids, progesterone, estrogens have decisive role in pregnancy and delivery, they directly or indirectly regulate most of molecular events involved in uterine physiology. Important paracrine regulators are prostaglandins, they are used clinically to induce abortion and stimulate parturition [6], the oxytocin and oxytocin receptor also play some but not decisive role in the regulation of myometrial function [7]. Further list of different other, endocrine or paracrine regulators in uterine function could be find in several recent reviews [2, 3, 6].

It has been long time known, that mechanical changes in the musculature are important regulator of myometrium. Two types of mechanical changes can be observed in myometrium during pregnancy; a sustained myometrial hypertrophy, hyperplasia and stretching due to 400-fold increase in uterine volume, and stepwise and continuous shortening due to 90% decrease in the uterus volume during labour [8]. Parallel to mechanical changes different endocrine and paracrine hormones, regulators are activated forming the complex network, which finally regulate and maintain the most optimal environment in the uterus. No data are available regarding the calorimetric characteristics of the myometrium. The aim of present study is to have insight in these biophysical characteristics which may let to gain more information of myometrial function at different reproductive states.

Experimental

Materials and methods

Sample preparation

Pregnant myometrium were obtained at cesarean delivery from six pregnant women. At the time of cesarean section in pregnant women full thickness strips of term

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myometrial tissue were excised from upper margin of the transverse uterine incision. Myometrial tissue was obtained in same manner from uteri of two non-pregnant women undergoing hysterectomy for benign disorder. Tissue samples were frozen and reserved in liquid nitrogen until calorimetric investigation.

The Institutional Human Studies Committee approved the use of the tissues and informed consent was obtained from the patients.

DSC measurements

Thermal unfolding of uterus strips from myometria was monitored by a Setaram Micro DSC-II calorimeter. Conventional Hastelloy batch vessels were used during the denaturation experiments with 650 μL sample volume (uterus strips plus Hanks buffer) in average. Typical uterus probe wet masses for calorimetric experiments varied between 150–200 mg. Hanks Balanced Salts (HBSS; Sigma, St. Louis, Missouri, USA) buffer was used as a reference sample. The sample and reference vessels were equilibrated with a precision of ±0.1 mg. The repeated scan of denatured sample was used as baseline reference, which was subtracted from the original DSC curve.

Evaluation of DSC measurements

Calorimetric enthalpy from thermograms of myometrial samples was determined using Setaram two point fitting integration program. The melting temperatures (T_m) and the half-width of endothermic peaks ($T_{1/2}$) were used for further thermal characterization of denaturation.

Results and discussion

We have examined the myometrium from uteri of healthy postmenopausal and of cyclic hyperoestrogenic women and these were compared with uteri of pregnant patients with different gestational age (Table 1). In case of menopause we have observed the main melting of sample at T_m=63.1°C with 3.4°C as half-width of transition temperature ($T_{1/2}$) and 0.98 J g^{-1} calorimetric enthalpy, while in excess oestrogen state of uterus the same parameters were: T_m=60.6°C with 4.5°C as half-width of transition temperature and 0.69 J g^{-1} calorimetric enthalpy (Fig. 1 and Table 2). These data could refer to the more rigid structure of uterus in menopause (smaller half-width is the sign of stronger cooperativity of structural subunits) compared with the 'active' ($T_{1/2}$=4.5°C) one.

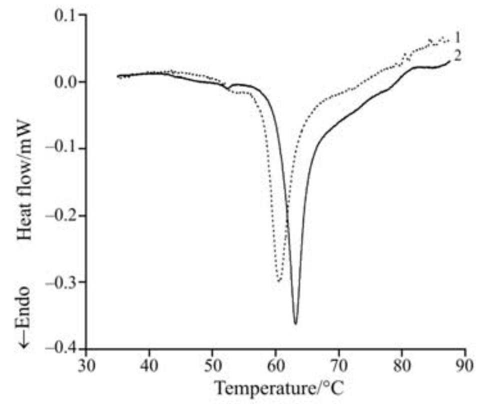

Fig. 1 Thermal denaturation of human uteri in post menopause and excess oestrogen states (for symbols see Table 1)

In case of pregnant myometrium the calorimetric enthalpy significantly increased with the gestational age (Table 2), which could be the consequence of the more ordered and 'packed' structure of the uterus wall because of the increased tension evoked by the enlargement of the uterus (Fig. 2).

The calorimetric enthalpy was the smallest in case of gravidity of 34 weeks (Table 2) and increased up to 41 weeks (from 0.44 to 0.79 J g^{-1}). It was very interesting that in certain cases e.g.: in case of prolapsed of placenta at the 31st gestational week (1.13 J g^{-1}) or at prolonged labour at the 41st gestational week (1.34 J g^{-1}) we have observed standing out calorimetric enthalpies (Fig. 3) for single childbirth and on the contrary in twin birth at the 36th gestational week we have detected the smallest one (0.37 J g^{-1}, Fig. 3 and Table 2 with bold letters). The gestational age dependence of calorimetric enthalpy could be explained by the increased ordering of mus-

Table 1 Profile of women from whom myometrial tissues was obtained

Sample	State	Gestational age/week	Complication
1	cyclic, non-pregnant	–	hyperoestrogenism
2	postmenopause	–	–
3	pregnant	31	placenta previa
4	pregnant	34	preeclampsia
5	pregnant	36	breech presentation
6	pregnant	36	gemini
7	pregnant	41	dystocia
8	pregnant	41	2 previous cesarian section in the history

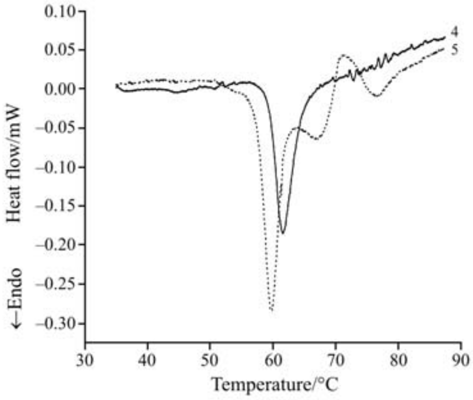

Fig. 2 Curves of uteri in case of premature birth

Table 2 Thermal parameters of gravid and non-gravid human uteri (ΔH stands for calorimetric enthalpy, T_m is the maximum denaturation temperature and $T_{1/2}$ is its half-width

Sample	Gestational age/ week	ΔH/ J g^{-1}	T_m/ °C	$T_{1/2}$/ °C
1	–	0.69	60.6	4.5
2	–	0.98	63.1	3.4
3	31	1.13	61.4	2.75
4	34	0.44	61.6	3.3
5	36	0.72	59.8	3.1
6	36	0.37	62.0	3.2
7	41	1.34	61.6	3.6
8	41	0.79	61.2	3.6

cle fibres in the wall of the uterus (this way they become more densely packed with increased heat capacity) because of the increasing tension caused by the enlargement of the uterus during the development of foetus. In case of prolapsed placenta we have to perform further experiments to find a possible explanation. The smallest calorimetric enthalpy in case of twin birth could be the extreme weakening of the wall of uterus and this way the less thermal stability because of the abnormal enlargement of uterus.

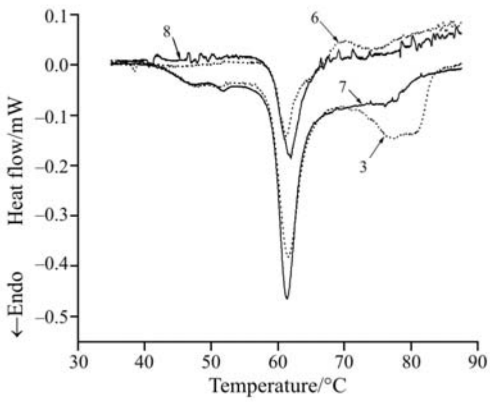

Fig. 3 DSC scans of uteri from 31st–41st weeks

To sum up we can say that the thermal analysis could be applied successfully in this new field of medical application too as it was done by us previously for other problems [9–13]. The obtained thermal parameters are in good correlation with the physiological states of uteri. Further experiment should be performed to find a correlation between thermal parameters and structural or functional changes of myometrium which bring us closer to understanding the myometrial function and its regulation during different physiological and pathophysiological events.

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